

Immunohistochemical Study of Epiretinal Proliferative Cellular Tissue From a Patient With Sarcoidosis

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Background: Sarcoidosis is a granulomatous disease causing uveitis. Although steroid therapy is usually effective for many patients, some are resistant to this therapy. In such cases, vitrectomy may be chosen as the therapeutic method to treat intraocular inflammation.

Case: A 26-year-old Japanese man was diagnosed as having sarcoidosis by clinical findings and histological examination of bronchoalveolar lavage.

Observations: One year after diagnosis, vitreous opacity worsened and pars plana vitrectomy (PPV) was performed. Six months later, recurrence of vitreous opacity appeared and severe retinal exudative changes with proliferative vitreoretinopathy developed. One year after the first operation, PPV was repeated and the epiretinal proliferative tissue was removed and examined.

Conclusions: Histologic examination of the specimen showed scattered noncaseating granulomatous inflammation mainly consisting of epithelioid histiocytes and lymphocytes. Plasma cells as well as T cells were identified and the predominance of CD8-positive T cells was demonstrated. Taking everything into consideration, a new finding of CD8 predominance in the epiretinal proliferative tissue was demonstrated. **Jpn J Ophthalmol 2002; 46:675–678** © 2002 Japanese Ophthalmological Society

Key Words: Bronchoalveolar lavage, CD8T cells, epiretinal proliferative tissue, sarcoidosis, vitrectomy.

Introduction

Sarcoidosis is a systemic granulomatous disease often occurring in the lung, skin, lymph nodes, or eye. Specimens from sarcoidosis patients have been obtained from many organs by bronchoalveolar lavage and skin biopsy. A number of reports suggest that T cells play an important role in the development of sarcoidosis. Uveitis is one of the important diagnostic criteria for sarcoidosis. Compared to other affected organs, much fewer reports are available concerning intraocular specimens from sarcoidosis patients.

Here we report on a sarcoidosis patient from whom a vitrectomized specimen was collected because of proliferative changes in the retina.

Case Report

Bilateral hilar lymphadenopathy was observed in a 26-year-old Japanese man. He had a past history of uveitis in his left eye. Thus, sarcoidosis was suspected. He was diagnosed as having sarcoidosis both histopathologically, by bronchoalveolar lavage, and clinically, by tuberculin skin test, as well as by testing for high serum angiotensin-converting enzyme and high serum IgG concentration. One month after bronchoalveolar lavage, he started to receive systemic prednisolone (total 1500 mg) because of vitreous opacity with hemorrhage in his left eye. His cor-

Received: November 27, 2001

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rected visual acuity improved from 0.5 to 1.0. One year after the onset, vitreous opacity with retinal exudative changes increased and he was treated with prednisolone again, but not as effectively as before. At this time, corrected visual acuity in his left eye was 0.2. Therefore, pars plana vitrectomy (PPV) was performed without lens extraction because the proliferative vitreoretinal changes were minimal at that time. Visual acuity improved to 0.6. Meanwhile, the inflammation was controlled by systemic prednisolone.

Six months after the first operation, there were signs of the development of the massive retinal exudative changes with proliferative vitreoretinopathy. One year after the first operation, it was necessary to perform vitrectomy and resection of the epiretinal membrane with lens extraction, intraocular lens (PC-IOL, PMMA) implantation and the scleral buckling procedure with encircling band, because traction as well as exudative retinal detachment developed.

The epiretinal proliferative tissue obtained by PPV (Figure 1) was fixed in 10% buffered formalin and embedded in paraffin for either light microscopic or immunohistochemical examination. A 6- μ m section was cut and the conventional method was performed for immunohistological studies. The antibodies used were anti-CD4, anti-CD8, anti-macrophage, anti-S100 protein, and anti-MHC class II. As shown in Figure 2A, granulomatous tissues accompanied by accumulation of lymphocytes were identified. Necrotic changes were not seen in the granulomatous lesions. Macrophages were identified either in the granuloma or in the area of lymphocyte accumula-



Figure 1. Photograph of epiretinal proliferative tissue obtained during pars plana vitrectomy in a Japanese man with sarcoidosis.

tion. Half of the lymphocytes were plasma cells. The major component of the rest of the infiltrating cells were T cells with CD8-positive T cells predominating (Figure 2B) compared to CD4-positive T cells (Figure 2C). Both CD4-positive and CD8-positive cells were surrounding the granulomatous region (Figures 2B and 2C). S100 protein-positive cells, which are known to be dendritic cells in certain circumstances, were few. Macrophages and MHC class II-positive cells were dominantly detected within the area of the granuloma.

After this second PPV, traction retinal detachment developed again, and PPV, laser photocoagulation and removal of the IOL with silicone oil injection were performed. One month later, SF6 gas injection was performed following removal of the silicone oil. Up to the present, the retina in the posterior pole is attached and corrected visual acuity in the left eye is 0.02.

Discussion

Sarcoidosis, a granulomatous disease, is one of the most common diseases causing uveitis. The etiology of sarcoidosis is still unknown but steroid therapy is generally effective. Yet, in some patients with sarcoidosis, steroid therapy is ineffective. In those cases, vitrectomy might have to be chosen for treatment of the intraocular inflammation in sarcoidosis patients. Although several reports¹ have demonstrated that lymphocytic infiltration is dominant in the intraocular specimens, detailed immunohistological analysis was not reported.

We present immunohistological findings on the epiretinal proliferative tissue from a patient with sarcoidosis. In this report, we obtained the new finding of CD8 predominance in the inflammatory site. Notable findings reported here are: (1) CD8-positive cells, compared with CD4-positive cells, were predominant in the epiretinal granulomatous lesions; and (2) CD4-positive and CD8-positive cells were surrounding the granulomatous regions. These findings are in accord with the previous report² that both CD4 and CD8 T cells infiltrated the inflammatory sites of the lung, and CD8 T cells surrounded the granuloma. In their report,² CD8-positive T cells were present in abundance in the outer boundaries of the granuloma, while CD4-positive T cells were detected in the internal area and surrounding areas of the granuloma. In contrast, in this case, no clear difference was noted in the distribution between CD4 and CD8 T cells. It is noteworthy that the tissue was harvested 1 year after the first PPV, and this

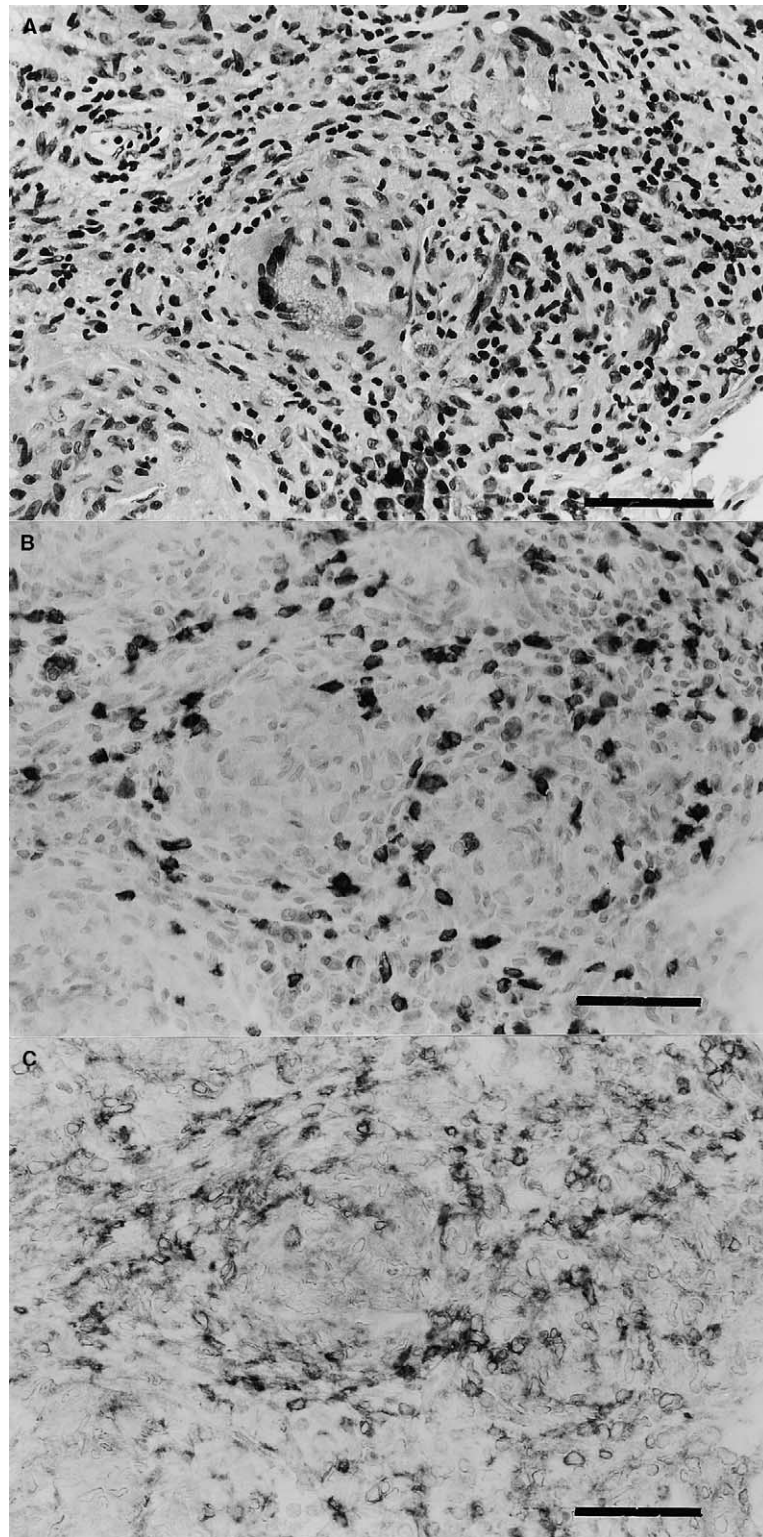


Figure 2. Histologic section of preretinal proliferative tissue from the left eye. (A) Granuloma formation with lymphocytic infiltration was noted (hematoxylin and eosin stain). Bar = 80 μ m. (B) Infiltration of CD8+ cells surrounding the granulomas. Bar = 40 μ m. (C) Less infiltration of CD4+ cells than CD8+ cells. Bar = 40 μ m.

may be the reason why more CD8- than CD4-positive T cells were detected and distribution was similar between CD4- and CD8-positive cells. It could also be considered that the CD8-positive T cells may have gathered to suppress the local inflammation, because the CD8 phenotype is sometimes considered to represent suppressor cell markers.³ Interestingly, activated T cells were identified in epiretinal membranes from patients with proliferative diabetic retinopathy.⁴ Thus, T cells might have gathered nonspecifically into the remodeling sites of inflammation. There have been reports about the specimens of epiretinal or retinal tissues from patients with sarcoidosis after the initial surgery.^{1,5} However, no reports have been available concerning the immunohistochemical examination of a specimen from the epiretinal tissue of a patient with sarcoidosis who had already received PPV twice. Therefore, this re-

port might be valuable in considering the course of this disease.

References

1. Martin DF, Chan CC, de Smet MD, et al. The role of chorioretinal biopsy in the management of posterior uveitis. *Ophthalmology* 1993;100:705-714.
2. Kita S, Tsuda T, Sugisaki K, Miyazaki E, Matsumoto T. Characterization of distribution of T lymphocyte subsets and activated T lymphocytes infiltrating into sarcoid lesions. *Intern Med* 1995;34:847-855.
3. Ciobotariu R, Colovai AI, Pennesi G, et al. Specific suppression of human CD4+ Th cell responses to pig MHC antigens by CD8+CD28- regulatory T cells. *J Immunol* 1998;161:5193-5202.
4. Tang S, Le-Ruppert KC. Activated T lymphocytes in epiretinal membranes from eyes of patients with proliferative diabetic retinopathy. *Graefes Arch Clin Exp Ophthalmol* 1995;33:21-25.
5. Miyao A, Ikeda T, Matsumoto Y, et al. Histopathological findings in proliferative membrane from a patient with sarcoid uveitis. *Jpn J Ophthalmol* 1999;43:209-212.